

WE CLAIM

1. An isolated mTOR-associated protein (mTOR-AP) polypeptide comprising an amino acid sequence selected from the group consisting of:
  - (a) an amino acid sequence at least 70% identical to the amino acid sequence depicted in SEQ ID NO: 3;
  - (b) an amino acid sequence at least 70% identical to the amino acid sequence depicted in SEQ ID NO: 6;
  - (c) an amino acid sequence encoded by a nucleic acid that hybridizes under high stringency conditions to a complement sequence of the nucleic acid depicted in SEQ ID NO: 2.
  - (d) an amino acid sequence encoded by a nucleic acid that hybridizes under high stringency conditions to a complement sequence of the nucleic acid depicted in SEQ ID NO: 5.
2. The isolated polypeptide of claim 1, comprising an amino acid sequence at least 90% identical to the amino acid sequence depicted in SEQ ID NO: 3 or 6.
3. The isolated polypeptide of claim 1, wherein the isolated polypeptide is a variant of a polypeptide represented by SEQ ID NO: 3 or 6.
3. The isolated polypeptide of claim 1, wherein the isolated polypeptide is a fragment of a polypeptide represented by SEQ ID NO: 3 or 6.
4. The isolated polypeptide of claim 1, wherein the isolated polypeptide is a G protein  $\beta$  subunit Like protein (G $\beta$ L) polypeptide having an amino acid sequence represented by SEQ ID NO: 6.
5. The isolated polypeptide of claim 1, wherein the isolated polypeptide is a rapamycin-insensitive companion of mTOR (rictor) polypeptide having an amino acid sequence represented by SEQ ID NO: 3.

6. An isolated antibody, or fragment thereof, which is specifically immunoreactive with an epitope of an amino acid sequence represented by SEQ ID NO: 3 or 6.
7. The antibody of claim 6, wherein said antibody is selected from the group consisting of: a polyclonal antibody, a monoclonal antibody, an Fab fragment and  
5 a single chain antibody.
8. An isolated nucleic acid comprising a nucleic acid sequence selected from the group consisting of:
  - (a) a nucleic acid sequence at least 70% identical to the nucleic acid sequence depicted in SEQ ID NO: 2;
  - 10 (b) a nucleic acid sequence at least 70% identical to the nucleic acid sequence depicted in SEQ ID NO: 5;
  - (c) a nucleic acid sequence which is a complement of SEQ ID NO: 2;
  - (d) a nucleic acid sequence which is a complement of SEQ ID NO: 5;
  - (e) a nucleic acid sequence that hybridizes under high stringency conditions to a  
15 nucleic acid depicted in SEQ ID NO: 2, or to its complement; and
  - (f) a nucleic acid sequence that hybridizes under high stringency conditions to a nucleic acid depicted in SEQ ID NO: 5, or to its complement.
9. The nucleic acid of claim 8, comprising a nucleic acid sequence at least 90% identical to the nucleic acid sequence depicted in SEQ ID NO: 2 or 5.
- 20 10. The nucleic acid of claim 8, comprising a nucleic acid sequence that, due to the degeneracy of the genetic code, encodes the amino acid sequence encoded by the nucleic acid sequence depicted in SEQ ID NO: 2 or 5.
11. The nucleic acid of claim 8, wherein the nucleic acid encodes a G $\beta$ L polypeptide.
12. The nucleic acid of claim 11, comprising a nucleic acid sequence depicted in SEQ  
25 ID NO: 4 or 5.

13. The nucleic acid of claim 8, wherein the nucleic acid encodes a rictor polypeptide.
14. The nucleic acid of claim 13, comprising a nucleic acid sequence depicted in SEQ ID NO: 1 or 2.
15. A vector comprising a nucleic acid sequence encoding an mTOR-AP polypeptide that is at least 70% identical to the polypeptide represented by SEQ ID NO: 3 or 6.
16. The vector of claim 15, wherein the nucleic acid is operably linked to a transcriptional regulatory sequence.
17. An isolated host cell comprising a nucleic acid of claim 8.
18. The isolated host cell of claim 17, wherein the nucleic acid is a vector.
19. A method of producing an mTOR-AP polypeptide comprising culturing the host cells of claim 17 under conditions suitable for expression of the mTOR-AP polypeptide, wherein the mTOR-AP polypeptide is thereby produced.
20. The method of claim 19, wherein the mTOR-AP polypeptide is a GβL polypeptide.
21. The method of claim 19, wherein the mTOR-AP polypeptide is a rictor polypeptide.
22. A method for detecting the presence of an mTOR-AP polypeptide of claim 1 in a sample, comprising:
  - (a) contacting the sample with an antibody which selectively binds to the polypeptide of claim 1; and
  - (b) determining whether the antibody binds to the polypeptide in the sample.

23. The method of claim 22, wherein the mTOR-AP polypeptide is a GβL polypeptide.
24. The method of claim 22, wherein the mTOR-AP polypeptide is a rictor polypeptide.
- 5 25. A kit for detecting an mTOR-AP polypeptide comprising:  
(a) an antibody of claim 3; and  
(b) a detectable label for detecting said antibody.
26. The kit of claim 25, wherein the mTOR-AP polypeptide is a GβL polypeptide.
27. The kit of claim 25, wherein the mTOR-AP polypeptide is a rictor polypeptide.
- 10 28. A method for detecting the presence of the nucleic acid of claim 8 in a sample, comprising:  
(a) contacting the sample with a probe or primer nucleic acid of claim 8; and  
(b) determining whether the probe or primer nucleic acid binds to a nucleic acid in  
15 the sample.
29. The method of claim 28, wherein the nucleic acid encodes a GβL polypeptide.
30. The method of claim 28, wherein the nucleic acid encodes a rictor polypeptide.
31. A kit comprising the probe or primer nucleic acid of claim 8 and instructions for use.
- 20 32. The kit of claim 31, wherein the probe or primer is for detecting a nucleic acid encoding a GβL polypeptide.
33. The kit of claim 31, wherein the probe or primer is for detecting a nucleic acid encoding a rictor polypeptide.

34. An isolated, purified or recombinant complex comprising an mTOR polypeptide and an mTOR-associated protein (mTOR-AP).

35. The complex of claim 34, wherein the mTOR-AP polypeptide is a GβL polypeptide.

5

36. The complex of claim 34, wherein the mTOR-AP polypeptide is a rictor polypeptide.

37. The complex of claim 35, further comprising a Raptor polypeptide.

10

38. The complex of claim 36, further comprising a GβL polypeptide.

39. A method for identifying a compound which modulates activity of an mTOR-AP polypeptide, comprising:

15

(a) contacting a polypeptide according to claim 1 with a test agent; and

(b) monitoring for modulation of mTOR-AP activity,

wherein a compound which modulates mTOR-AP activity is thereby identified.

40. The method of claim 39, wherein the mTOR-AP polypeptide is a GβL polypeptide.

20

41. The method of claim 40, wherein the GβL activity monitored in step (b) is binding of a GβL polypeptide to an mTOR polypeptide.

42. The method of claim 40, wherein the GβL activity monitored in step (b) is stabilization of the interaction between raptor and mTOR.

25

43. The method of claim 40, wherein the GβL activity monitored in step (b) is activation of mTOR kinase activity.

30

44. The method of claim 39, wherein the mTOR-AP polypeptide is a rictor polypeptide.

45. The method of claim 44, wherein the rictor activity monitored in step (b) is  
5 binding of a rictor polypeptide to an mTOR polypeptide.

46. The method of claim 44, wherein the rictor activity monitored in step (b) is the phosphorylation state of Protein Kinase  $\alpha$  (PKC $\alpha$ ).

10 47. The method of claim 44, wherein the rictor activity monitored in step (b) is the organization of the actin cytoskeleton.

48. A method of inhibiting aberrant activity of an mTOR-AP-expressing cell,  
comprising contacting the cell with a compound that modulates the activity or  
15 expression of the polypeptide of claim 1, in an amount which is effective to  
reduce or inhibit the aberrant activity of the mTOR-AP.

49. The method of claim 48, wherein the compound is selected from the group  
consisting of a peptide, a phosphopeptide, a small organic molecule, an antibody,  
20 and a peptidomimetic.

50. The method of claim 48, wherein the cell is a cancer cell.

51. The method of claim 48, wherein the cell is a human cell.  
25

52. A method of treating or preventing a disorder that is responsive to mTOR-AP  
modulation, in a subject, comprising administering to the subject an effective  
amount of a compound that modulates the activity or expression of the  
polypeptide of claim 1.  
30

53. The method of claim 52, wherein the disorder is characterized by aberrant activity of an mTOR-AP, and the compound reduces or inhibits the aberrant activity of the mTOR-AP.

5 54. The method of claim 52, wherein the mTOR-AP is GβL.

55. The method of claim 52, wherein the mTOR-AP is rictor.

56. The method of claim 52, wherein the disorder is cancer.

10

57. The method of claim 52, wherein the disorder is diabetes.

58. A transgenic mouse having germline and somatic cells comprising a chromosomally incorporated transgene that disrupts the genomic mTOR-AP gene and inhibits expression of said gene, wherein said disruption comprises insertion of a selectable marker sequence resulting in said transgenic mouse exhibiting increased susceptibility to the formation of tumors as compared to the wildtype mouse.

15

20 59. The transgenic mouse of claim 58, wherein the mTOR-AP is GβL.

60. The transgenic mouse of claim 58, wherein the mTOR-AP is rictor.